

PESFDGDPASNTAPLQPE, SEQ ID NO. 7, or a functional equivalent thereof;
LYISAWPDSLPLDSVFNQLQ, SEQ ID NO. 8, or a functional equivalent thereof;
LFRNPHQALLHTANRPEDE, SEQ ID NO. 9, or a functional equivalent thereof;
CLPCHPECQPQNGSVTCFGPEADQCVACAHYKDP, SEQ ID NO. 10, or a functional
equivalent thereof;
KPDLSYMPIWKFPDEEGA, SEQ ID NO. 11, or a functional equivalent thereof;
INGTHSCVDLDDKGCPAEQRAS, SEQ ID NO. 12, or a functional equivalent thereof; and
INGTHSCVDLDDKGCPAEQR, SEQ ID NO. 42, or a functional equivalent thereof.

REMARKS

By the present amendment, Applicants are hereby amending the specification (i) to correct an obvious typographical error in Table 1, (ii) to correct an obvious typographical error in the sequence of SEQ ID NO. 42 as it appears in claims 31 and 32 of the present application, and (iii) to provide a substitute Sequence Listing which also contains a corrected sequence for SEQ ID NO. 42. By the present amendment, applicants are also amending claim 6 to make it consistent with claim 31.

The typographical error in Table 1 is the designation "DW4" before the final sequence. By the present amendment the term "DW4" has been deleted from Table 1. DW4 is described in the specification as being amino acid 628 through amino acid 647 of the HER-2 protein. (See page 34, lines 15-17 of the specification.) Since SEQ ID NO. 12 comprises amino acid 628 through amino acid 650 of the HER-2 protein, it is not DW4. Thus, the amendment to Table 1 adds no new matter.

The typographical error in SEQ ID NO. 42 as it appears in claims 31 and 32 is the omission of an R at the C terminus. SEQ ID NO. 42 is the amino acid sequence of the HER-2 peptide that is incorporated into MVFDW4. As noted on page 34, lines 15-22 of the specification, MVFDW4 is described as comprising amino acid 628 through amino acid 647 of the HER-2 protein with the substitution of a G for the C at position 630. A peptide which comprises amino acid 628-647 of the HER-2 protein is at least 20 amino acids in length. The peptide of SEQ ID NO. 42 as it was erroneously presented in claims 31 and 32 is only 19 amino acids in length. The peptide of SEQ ID NO. 42, as it was erroneously presented in claims 31 and 32 does not include the arginine at position 647. (See final sequence (i.e., amino acid 628 through amino acid 650 of HER-2) in Table 1 of the specification.) To correct this obvious

error applicants have added an arginine to the C-terminus of SEQ ID NO. 42, as it appears in claims 31 and 32.

The peptide of SEQ ID NO. 42 as it was erroneously presented in the Sequence Listing mailed to the Patent Office on July 3, 2002 is 23 amino acids in length. The peptide of SEQ ID NO. 42 as it erroneously appears in the Sequence Listing filed on July 3, 2002 contains amino acids 648-650 of the HER-2 protein. (See last sequence in Table 1 of the specification.) The typographical error in SEQ ID NO. 42 as it appears in the Sequence Listing mailed to the patent office on July 3, 2002 is the inclusion of an Ala, Ser, and Pro at the C terminus. To correct this obvious error, Applicants have deleted these additional amino acids from the C terminus of SEQ ID NO. 42. The amendments add no new matter.

A document entitled "VERSION WITH MARKINGS TO SHOW CHANGES MADE" showing the additions as underlined and the deletions in brackets is attached hereto.

Applicant respectfully requests entry of the present Preliminary Amendment and the Substitute Sequence Listing.

Respectfully submitted,

Date: December 2, 2002

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE SPECIFICATION:

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Table 1. Consolidated Human p185 HER-2 predicted B cell epitopes listed in the order of ranking by amino acid residue numbers. Asparagine (N)-linked glycosylation sites are underlined in bold.

Predictive Ranking	Residue	Amino Acid Sequence	Secondary Structure
7	27 – 45	Tgtdmklrlpaspethldm	25 – 28 β turn; 29 – 32 α helix; 35 – 38 β turn
8 (DW5)	115 – 136	AVLDNGDPL <u>NNT</u> TPVTGASPGG	116 – 135 β turn
9	168 – 189	LWKDIFHKNNQLALTLIDT <u>NRS</u>	173 – 176 β turn; 177 – 181 α helix
1	182 – 216	TLIDT <u>NRS</u> RACHPCSPMCKGSRCWG ESSEDCQSLT	184 – 212 β turn/loop
6	270 – 290	ALVTYNTDTFESMPNPEGRT	273 – 286 β turn; 278 – 280 α helix
3	316 – 339	PLHNQEVTAEADGTQRAEKCSKPCA	319 – 324 α helix; 324 – 336 β turn.
10 (DW1)	376 – 395	PESFDGDPASNTAPLQPE	379 – 388 β turn
12 (DW6)	410-429	LYISAWPDSLPLDSVFQNLQ	413-421 β turn
2	485 – 503	LFRNPHQALLHTANRPEDE	497 – 500 β turn; 499 – 504 α helix
11	560 – 593	CLPCHPECQPQ <u>NGSV</u> TCFGPEADQCVACAH YKDP	561 – 572 & 589 – 593 β turn; 579 – 581 α helix
4	605 – 622	KPDLSYMPIWKFPDEEGA	616 – 620 α helix
5 [(DW4)]	628 – 650	IN <u>G</u> THSCVDLDDKGCPAEQRASP	635 – 642 β turn; 643 – 646 α helix

IN THE CLAIMS:

6. (Twice Amended) A composition for stimulating an immune response to HER-2 protein, wherein said composition is a multivalent peptide and comprises 2 or more HER-2 B cell epitopes, a Th cell epitope, and a template;

wherein said 2 or more HER-2 B cell epitopes are different, and wherein each of said 2 or more HER-2 B cell epitopes is from 15 to 40 amino acids in length and comprises a sequence selected from the group consisting of:

TGTDMLRLPASPETHLDM, SEQ ID NO. 1, or a functional equivalent thereof;
 AVLDNGDPLNNTTPVTGASPGG, SEQ ID NO. 2, or a functional equivalent thereof;
 LWKDIFHKNNQLALTLIDTNRS, SEQ ID NO. 3, or a functional equivalent thereof;
 TLIDTNRSRACHPCSPMCKGSRGWGESSEDCQSLT, SEQ ID NO. 4, or a functional
 equivalent thereof;
 ALVTYNTDTFESMPNPEGRT, SEQ ID NO. 5, or a functional equivalent thereof;
 PLHNQEVTAEDGTQRAEKCSKPCA, SEQ ID NO. 6, or a functional equivalent thereof;
 PESFDGDPASNTAPLQPE, SEQ ID NO. 7, or a functional equivalent thereof;
 LYISAWPDSLPLDSVVFQNLQ, SEQ ID NO. 8, or a functional equivalent thereof;
 LFRNPHQALLHTANRPEDE, SEQ ID NO. 9, or a functional equivalent thereof;
 CLPCHPECQPQNGSVTCFGPEADQCVACAHYKDP, SEQ ID NO. 10, or a functional
 equivalent thereof;
 KPDSLMPYIWKFPDEEGA, SEQ ID NO. 11, or a functional equivalent thereof; [and]
 INGTHSCVDLDDKGCPAEQRAS, SEQ ID NO. 12, or a functional equivalent thereof; and
INGTHSCVDLDDKGCPAEQR, SEQ ID NO. 42, or a functional equivalent thereof;

wherein the HER-2 B cell epitopes and the Th cell epitope are attached to the template.

31. (Once Amended) The multivalent peptide of claim 6, wherein the multivalent peptide comprises a HER-2 B cell epitope which comprises INGTHSCVDLDDKGCPAEQR, SEQ ID NO. 42 or a functional equivalent thereof, a HER-2 B cell epitope which comprises SEQ ID NO. 6 or a functional equivalent thereof, and a HER-2 B cell epitope which comprises SEQ ID NO. 9 or a functional equivalent thereof

32. (Once Amended) A method of treating a subject with cancer comprising administering a mixture of chimeric peptides to the subject, wherein said mixture comprises 2 or more chimeric peptides, wherein each of said 2 or more chimeric peptides comprise a HER-2 B cell epitope, a T helper (Th) epitope; and a linker joining said HER-2 B cell epitope to said Th epitope; wherein the HER-2 B cell epitope of said 2 or more chimeric peptides are different, and comprise a sequence selected from the group consisting of:

TGTDMLRLPASPETHLDM, SEQ ID NO. 1, or a functional equivalent thereof;
 AVLDNGDPLNNTTPVTGASPGG, SEQ ID NO. 2, or a functional equivalent thereof;

LWKDIFHKNNQLALTLIDTNRS, SEQ ID NO. 3, or a functional equivalent thereof;
TLIDTNRSRACHPCSPMCKGSRGWGESSEDCQSLT, SEQ ID NO. 4, or a functional
equivalent thereof;
ALVTYNTDTFESMPNPEGRT, SEQ ID NO. 5, or a functional equivalent thereof;
PLHNQEVTAEDGTQRAEKCSKPCA, SEQ ID NO. 6, or a functional equivalent thereof;
PESFDGDPASNTAPLQPE, SEQ ID NO. 7, or a functional equivalent thereof;
LYISAWPDSLPLDSVFQNLQ, SEQ ID NO. 8, or a functional equivalent thereof;
LFRNPHQALLHTANRPEDE, SEQ ID NO. 9, or a functional equivalent thereof;
CLPCHPECQPQNGSVTCFGPEADQCVACAHYKDP, SEQ ID NO. 10, or a functional
equivalent thereof;
KPDLSYMPIWKFPDEEGA, SEQ ID NO. 11, or a functional equivalent thereof;
INGTHSCVDLDDKGCPAEQRAS, SEQ ID NO. 12, or a functional equivalent thereof; and
INGTHSCVDLDDKGCPAEQR, SEQ ID NO. 42, or a functional equivalent thereof.